

# Abstract

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Title of diploma thesis: Natural compounds isolated from plants at the Faculty of Pharmacy in Hradec Králové as potential inhibitors of aldo-ketoreductase 1A1 (AKR1A1)

Aldo-keto reductase 1A1 is an enzyme belonging to the aldo-keto reductase superfamily. It is a monomeric, cytosolic enzyme that is able to reduce carbonyl groups within a wide range of substrates. The enzyme is expressed in almost every tissue in the body, most represented in hepatocytes, renal cells and salivary glands, where it contributes to the reduction of endogenous substrates and the first phase of biotransformation of xenobiotics.

AKR1A1 catalyzes NADPH-dependent reduction of aldehydes and ketones to their corresponding primary and secondary alcohols. Enzyme substrates include, for example, mevalonate; anthracycline antibiotics doxorubicin or daunorubicin; some pro-carcinogens that are activated by the reaction into carcinogens, such as: *trans*-dihydrodiol metabolites of polycyclic aromatic hydrocarbons. Generally, it is involved in the metabolism of lipids and carbohydrates that contain an aldehyde function. The increased expression and activity of AKR1A1 has been found in radioresistant laryngeal tumor cells, so it can be assumed that a potential enzyme inhibitor could increase the susceptibility of tumor cells to administered drugs, particularly anthracyclines.

In this diploma thesis the effectiveness of potential inhibitors was investigated. The investigated potential inhibitors of AKR1A1 were natural compounds isolated from plants at the Department of Botany of the Pharmaceutical Faculty in Hradec Králové. Specifically, these were the alkaloids of the plants Amaryllidaceae, Papaveraceae, Fumaridaceae and Berberidaceae. Incubation of AKR1A1 with individual potential inhibitors was performed, daunorubicin was used as the substrate, the amount of daunorubicinol was determined by means of the method of high effective liquid chromatography.